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The interference effect in arithmetic fact solving: an fMRI study

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Abstract

Some multiplication facts share common digits with other, previously learned facts, and as a result, different problems are associated with different levels of interference. The detrimental effect of interference in arithmetic facts knowledge has been recently highlighted in behavioral studies, in children as well as in adults, both in typical and atypical development. The present study investigated the brain regions involved in the interference effect when solving multiplication problems. Twenty healthy adults carried out a multiplication task in an MRI scanner. The event-related design comprised problems whose interference level and problem size were manipulated in a 2x2 factorial design. After each trial, individuals were requested to indicate whether they solved the trial by retrieving the answer from long-term memory. This allowed us to examine which brain areas were sensitive to the interference effect and problem size effect as well as the retrieval strategy. The results highlighted two specific regions: the left angular gyrus was more activated for low interfering than for high interfering problems, and the right intraparietal sulcus was more activated for large problems than for small problems. In both regions, brain activity was not modulated by the other effect. These results suggest that the left angular gyrus is sensitive to the level of interference of the multiplication problems, whereas previously this region was thought to be more activated by small problems or by retrieval strategy. Here, in a design manipulating interference and problem size, whilst controlling for retrieval strategy, we showed that it rather reflects an automatic mapping between the problem and the answer stored in long-term memory. The right intraparietal sulcus was modulated by the problem size effect, which supports the idea that the problem size effect comes from the higher overlap between magnitude of the answers of large problems compared to small ones. Importantly, neither effects can be reduced to a strategy effect since they were present when analyzing only retrieval trials.

Keywords: interference effect, arithmetic fact, multiplication, angular gyrus, intraparietal sulcus, numerical cognition

1. Introduction

To live independently, numerical and arithmetical knowledge are indispensable to everyone. Consequently, research into numerical cognition, including identifying the brain regions involved and understanding dyscalculia, is a major theme in human cognitive neuroscience. Among different number processes, the capacity to learn and retrieve simple calculation problems has received substantial interest, first because it is essential for all more complex mathematical procedures, and second, because its impairment is a core feature of dyscalculia (Cho et al., 2012; De Smedt, Holloway, & Ansari, 2011; Jordan & Montani, 1997).

Through practice, simple calculation problems become stored in long-term memory and constitute an arithmetic facts network (e.g. McCloskey, Harley, & Sokol, 1991). Children start to solve simple problems by using quantity-based counting strategies and progressively store and therefore retrieve the answer of problems from long-term memory (e.g. Siegler, 1988). Among the four operations, simple additions and single-digit multiplications are known to more frequently trigger a retrieval strategy than two-digit problems or complex subtractions (Robinson et al., 2006; Roussel, Fayol, & Barrouillet, 2002; Thevenot, Castel, Fanget, & Fayol, 2010). Moreover, the multiplication tables are specifically trained during primary school, and are therefore assumed to be represented in long-term memory.

A robust characteristic of the arithmetic facts network is the problem size effect (De Brauwer, Verguts, & Fias, 2006). That is, better performance is observed for smaller problems compared to larger problems. The usual interpretation of this effect is that smaller problems are more often solved by retrieving the answer from long term memory than larger problems (Zbrodoff & Logan, 2005). Different explanations for this difference of performance between small and large problems have been suggested in the literature. First, some authors argued that frequency accounts for the problem size effect (Ashcraft, 1987; Ashcraft & Christy, 1995; McCloskey & Lindemann, 1992). For instance, Ashcraft and Christy (1995) reported that small problems are more often retrieved because they are more frequent in primary school books than larger problems are. Second, Siegler (1988) suggested that each problem is associated with all answers, correct and wrong, that have been reached in the past (Distribution of Association model). Critically, the probability of making an error increases as problem size increases, and therefore larger problems will be associated with more incorrect answers. Another model, based on the principles of cooperation and competition between neighboring arithmetic problems has been proposed by Verguts and Fias (2005). Their hypothesis is that the answers of the neighboring problems (e.g. 4 x 7, 4 x 5, 3 x 6, 5 x 6 are the neighbors of 4 x 6) compete or cooperate when retrieving the answer of a given problem. Neighbor answers that lead to the same response (because they have similar decade or unit) are consistent and will facilitate the retrieval of the correct answer, while inconsistent neighbors will compete and delay the retrieval of the correct answer. Since large problems possess more inconsistent neighbors than small problems, this could explain the problem size effect. Finally, the semantic representation of numbers has been suggested to account for the problem size effect (Campbell, 1995; Stoianov, Zorzi, Becker, & Umilta, 2002). For instance, the Network Interfering Theory, proposed by Campbell (1995), suggested that the problem size effect is the result of the magnitude representations of the problems' answers. These magnitude representations are known to follow a psychophysical scale that is more compressed as the magnitude increases (Dehaene, 1992). Accordingly, representation of answers of large magnitude would be more similar (closer) to one another than representations of answers of small magnitude.

Recently, another important effect that modulates performance in arithmetic facts solving has been described: the interference effect. Based on the feature overlap theory (Nairne, 1990), the similarity between multiplication tables has been suggested to trigger interference during the learning stage. In primary school, children are taught the multiplication tables from the two times table up to the nine times table. The hypothesis is that when children have to learn a problem, the quality of the memory representation of the problem will depend on the previously learned problems; the more similar the problem is to those already learned, the more this proactive interference will impact on its encoding. Based on this theory, De Visscher and Noël (2014b) calculated the similarity between multiplications by considering the common association of digits one problem shared with the already learned problems (from table 2 to table 9). This interference parameter aims at representing the weight of proactive interference that has been created during the learning stage for each problem. To compute the proactive interference that each problem receives from the previously learned problems, the authors sorted the 36 different problems from table 2 up to table 9. The proactive interference is measured based on the digit overlap between one problem (the combination of operands and product) with the previously learned problems. Each time that a combination of two digits of a given problem is present in a previously learned problem, one "proactive interference" point is added to the proactive interference weight of that given problem. For instance, when learning 3 x 9 = 27, proactive interference comes from 7 previously learned problems that share pair(s) of digits with the given problem (**3** x **2** = 6, **2** x **7** = 14, **9** x **2** = 18, **3** x 3 = **9**, 4 x **3** = 1**2**, **3** x **7** = **2**1, 8 x **3** = **2**4), resulting in a level of interference of 9 (three digits are shared with 3 x 7 = 21 adding 3 points to the 6 points coming from the other problems). The problem 5 x 5 = 25 is less interfering since it receives only 3 points of proactive interference from **2** x **5** = 10, 3 x **5** = 1**5** and 4 x **5** = **2**0. First, the authors showed that the interference parameter determined the difficulty across multiplication problems in third-grade children, fifth-grade children and adults, with greater interference leading to longer reaction times. Second, an individual's sensitivity to the interference parameter was calculated and the authors tested whether it contributed to between-subject differences in multiplication performance. The data revealed that the sensitivity to the interference parameter substantially predicted global ability to solve multiplication in both children and adults. Regarding the atypical development, people with an arithmetic facts deficit showed greater sensitivity to the interference parameter. This has been shown in a single-case study as well as in a group study with fourth-grade children tested twice, one year apart. Beyond a greater sensitivity to the interference parameter, these participants also showed hypersensitivity-to-interference in memory with non-numerical material (De Visscher & Noël, 2013, 2014a).

While the problem size effect has been investigated in children and adults, the brain regions involved in the interference effect in calculation are not known. There are at least two important reasons for characterizing the brain regions associated with the interference effect. First, people with arithmetic facts dyscalculia show heightened sensitivity to interference. Identifying brain areas sensitive to the interference effect would shed light on the arithmetic facts deficit in dyscalculia. Second, studying the brain regions involved in the interference effect would enable a finer grained description of the different brain areas implicated in simple calculation solving than has been previously possible.

Previous research on the brain networks underpinning arithmetic calculation has identified numerous regions such as the angular gyri, intraparietal sulci, inferior and middle frontal gyri, supplementary motor areas and anterior cingulate gyri (see Menon, 2014 for a review). Among these areas, the intraparietal sulci are suggested to be involved in the magnitude representation of numbers and activity is these regions is modulated by the problem size effect (De Smedt et al., 2011; Dehaene, Piazza, Pinel, & Cohen, 2003;

Stanescu-Cosson, Pinel, van de Moortele, et al., 2000). The involvement of a large fronto-parietal network is observed when using a procedural strategy, compared to a retrieval strategy (Grabner et al., 2009). Grabner and colleagues (2009) proposed that the parietal regions are responsible for the magnitude representations and the frontal areas reflect the working memory and executive control demand. In children, the left hippocampus has been shown to be involved in the learning of multiplication facts (De Smedt, Holloway, & Ansari, 2011). This region is known to be implicated in learning, particularly in associative memory tasks (Eichenbaum, Otto, & Cohen, 2010; Squire, 1992; Yonelinas, 2002). After the learning phase, the arithmetic fact retrieval is supported by the angular gyrus (De Smedt et al., 2011; Grabner et al., 2009). Angular gyrus deactivation is greater for large than small problems (reverse problem size effect), and for untrained compared to trained problems (Delazer et al., 2003; Ischebeck et al., 2006; Stanescu-Cosson, Pinel, van de Moortele, et al., 2000; Wu et al., 2009). Recently, the angular gyrus has been suggested to mediate the automatic mapping of arithmetic problems onto answers stored in memory (Grabner, Ansari, Koschutnig, Reishofer, & Ebner, 2013). In this study, the left angular gyrus showed higher activation during confusing verification problems (e.g. 9 x 6 = 15, where the answer is the correct answer of the corresponding addition) compared to non-confusing verification problems (e.g. 3 + 8 = 26).

The current study aims at investigating the brain regions involved in the interference effect in multiplication solving; an effect that has been demonstrated in both children and adults and which has been shown to be distinct to the problem size effect (De Visscher & Noël, 2013, 2014a, 2014b). To this end, twenty healthy adults carried out a multiplication verification task in the scanner. In an event-related design, interference level and problem size were manipulated in a 2x2 factorial design. This allowed us to investigate whether the interference effect involved different brain regions compared to that of the problem size effect or whether the brain activation reveals a general difficulty effect. Furthermore, after each problem the participant reported whether he/she used a retrieval strategy. This enabled us to test whether the interference and the problem size effects are present above and beyond a strategy switch (specifically, retrieval for small/low interfering problems versus procedural strategies for large/high interfering problems, Zbrodoff & Logan, 2005) by analyzing both effects on the retrieved trials only.

2. Method

2.1 Participants

Participants were 20 right-handed healthy adults (10 females) aged between 23 and 34 years (mean ± SD: 29 ± 3.5). All participants were native English speakers with no neurological condition nor dyslexia or dyscalculia. They received £15 for their participation. The study was approved by the Brighton and Sussex Medical School's Research Governance and Ethics Committee.

2.2 Materials and procedure

Participants were given the task instructions outside of the scanner. Whilst in the scanner, the participants were asked to perform a multiplication verification task lasting about 30 minutes. After scanning, participants carried out a multiplication production task lasting 10 minutes.

2.2.1 fMRI design and procedure

The experiment in the scanner was a multiplication verification task. Following a brief fixation cross, each trial started with the presentation of a multiplication problem (Figure 1). Participants were given 3 seconds to retrieve the answer, after which they were shown a proposed solution (probe) and had to indicate whether this answer was a "true" or "false" solution to the presented problem. Responses were made by pressing one of two MRI compatible response buttons with the index or middle finger of the right hand (response-to-finger mappings were counterbalanced between participants and a reminder of this mapping was displayed on screen during the response phase). Participants had a maximum of 2 s to make a response and trials were coded as having an incorrect response when no button press was made within the 2 second window. Immediately after verifying each probe, participants were asked to report whether they had used a retrieval strategy to obtain the correct answer (via an index/middle finger button press). There was a 2 second response window for this question. The inter-trial interval (ITI) was jittered and lasted between 2 and 16 seconds (mean (SD): 6.34 ± 3.88).

During the pre-scan instructions, participants were urged to solve each problem (instead of passively waiting for the proposed answer). Participants were also told that a "retrieval strategy" is when they retrieve/recollect the answer directly from long-term memory without needing any further steps to reach the correct answer. Examples were provided to ensure that participants understood this before scanning commenced. The task was carried out in two parts with a break of up to 30 seconds between parts (participants could end the break sooner if they wished). Functional MRI scans were acquired in a single sequence including both runs and the break.

There were two main factors under investigation, the interference effect and the problem size effect, each with two levels of difficulty (high versus low interference and large versus small problems), yielding four experimental conditions in a 2x2 factorial design. Stimuli were drawn from the 36 possible combinations of operands from 2 to 9 (without the commutative pairs). The product and the proactive interference parameter (see De Visscher & Noël, 2014b) were used respectively as measures of the size and the interference of the problems. Six problems were allocated to each of the four conditions such that problem size and interference were orthogonal to each other. The 24 problems used, their associated products and interference parameters and the experimental groups that they were allocated to, are shown in Appendix A.

Stimuli were presented in a rapid event-related design. An optimal combination of stimulus order and ITI was generated with the make_random_timing.py script included with the AFNI package (Cox, 1996). We selected from 10,000 potential designs the ordering with the smallest amount of un-modeled variance. Each of the 24 problems was presented six times during the experiment (36 trials per condition); three times being associated with the correct answer and three times being associated with an incorrect answer (operand-related answer, see the Appendix A). The order of the operands (large first versus small first) was counterbalanced within and between runs.

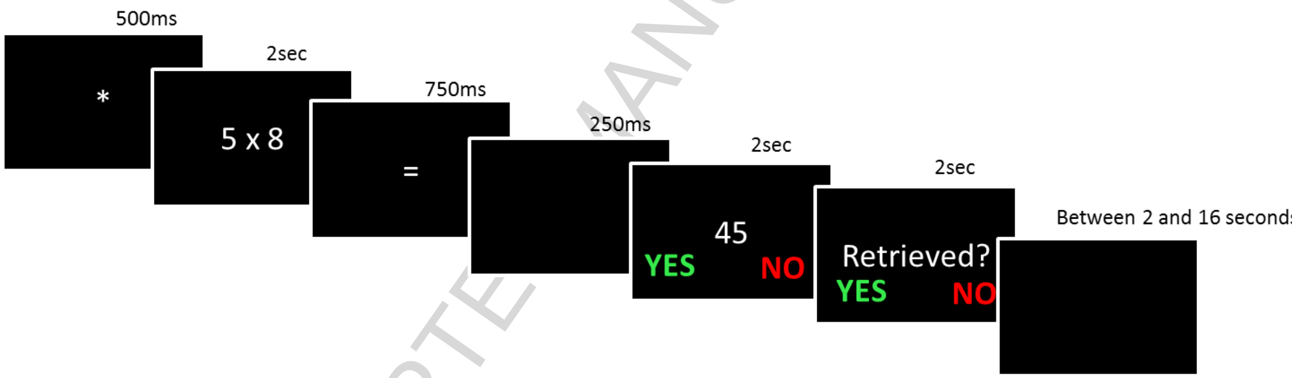


Figure 1: Time-course of one trial of the multiplication verification task used in the scanner.

2.2.2 *Subsequent behavioral task*

To allow a fine-grained analysis of each participant's ability to produce arithmetic facts, a multiplication production task was carried out after the scanning session. Participants were asked to say aloud the response of single-digit multiplications displayed one by one on the screen of a laptop (E-prime experimental software version 1.1, Psychology Software Tools). The problem remained until the participant responded in the voice key. The experimenter subsequently typed the answer and launched the next trial (voice key issues were coded). The 64 possible combinations of operands from 2 to 9 were used. The order of presentation was pseudo-randomized so that two successive trials never had the same operands or answer. The percentage of correct responses and the median reaction time (of the correct responses) were calculated for each participant.

2.2.3 *MRI acquisition*

All images were acquired on a 1.5 T Siemens Avanto scanner using a 32-channel phased-array head coil. Functional images were acquired using a T2*-weighted gradient-echo EPI sequence (TR = 2520 ms, TE = 43, flip angle = 90, FOV = 192x192 mm, matrix = 64x64). Each functional volume consisted of 34 contiguous 3.6 mm thick axial slices with 3x3 mm in-plane resolution. In addition, a high-resolution (1 mm³) T1-weighted whole brain anatomical volume was collected with a magnetization-prepared rapid gradient-echo (MP-RAGE) sequence for purposes of coregistration and standardization to a template brain. Finally, we collected a field map to allow for correction of geometric distortions induced by field inhomogeneities.

2.2.4 Image preprocessing

All preprocessing and statistical analyses of MRI data were carried out using SPM8 (Wellcome Department of Imaging Neuroscience, London, UK). First, each dataset was slice-time corrected, then simultaneously spatially realigned to the first volume and corrected for distortions due to field inhomogeneities using the Realign & Unwarp function in SPM. The resulting EPI volumes were registered to the anatomical scan and standardized through the application of the calculated transform between the anatomical scan and the MNI (Montreal Neurological Institute) template brain using the DARTEL toolbox (Ashburner, 2007). Finally, the EPI images were smoothed with an 8 mm FWHM gaussian kernel. The structural scans were normalized using the DARTEL toolbox in order to produce a mean image used to display statistical data with group level statistics. The anatomical labels were assigned by referencing to the Jüelich atlas from the Anatomy Toolbox in SPM (Eickhoff et al., 2005).

2.2.5 Data analyses

Two different first-level models of the fMRI data were produced in accordance with general linear principals. Model 1 grouped correctly verified problems into the four experimental conditions according to level of inference and problem size. Model 2 categorized correctly verified problems as either retrieved or non-retrieved depending on responses to the strategy question that followed multiplication verification. In each model, these periods of interest were specified as 3 second long boxcar functions (commencing at problem onset) and then convolved with SPM's canonical hemodynamic response function (HRF). Incorrectly verified problems and the rest periods between experimental runs were also modelled as regressors of no interest. As well as HRF amplitude estimates, temporal and dispersion derivatives were calculated on a voxel-wise basis. In addition, both models included 6 rigid-body movement parameters derived from the image realignment procedure. Furthermore, a 128 seconds high-pass filter was applied in each model to remove low frequency modulations such as scanner drift.

To examine group-wide BOLD differences as a function of interference and problem size, each individual's HRF amplitude estimates from the four experimental conditions (calculated in model 1) were entered into a 2x2 repeated measures ANOVA for a second-level analysis. Similarly, retrieved and non-retrieved HRF amplitude estimates (calculated in model 2) were entered into a paired-samples t-test to examine group-wide BOLD differences as a function of verification strategy.

3. Results

3.1 Behavioral data of the fMRI task

On average, participants provided a correct response on 94.79% of trials (SD = 5.37, range = 80.55 - 100%). Of these trials, a retrieval strategy was reportedly used on 69.72% (SD = 20.02) of occasions and a non-retrieval strategy on 24.76% (SD = 16.10) of occasions. No response was made to the retrieval strategy question on 5.52% (SD = 5.33) of correctly verified problems.

The mean accuracy (percentage of correct responses) for each condition is displayed in Table 1. A repeated-measures ANOVA on these data revealed a main effect of Problem size (performance was better on the small than on the large problems; $F(1,19) = 16.830$, $p = .001$, $\eta_p^2 = .470$) and a main effect of Interference (performance was better on the low interfering than on the high interfering problems; $F(1,19) = 14.878$, $p = .001$, $\eta_p^2 = .439$). No interaction was found ($F(1,19) = 2.862$, $p = .107$, $\eta_p^2 = .131$).

Table 1: Mean and standard deviation of accuracy per condition.

Mean (SD)	Accuracy	
	Low interference	High interference
Small	98.06 (2.40)	95.97 (6.47)
Large	95.28 (7.33)	89.86 (8.70)

The same ANOVA was run on the retrieval trials only (see Table 2). A main effect of interference indicated that low interference problems were better performed than high interference problems ($F(1,19) = 7.937$, p = .011, $\eta_p^2 = .295$). A main effect of size revealed that small problems led to higher accuracy than large problems ($F(1,19) = 5.267$, p = .033, $\eta_p^2 = .217$). No interaction was found ($F<1$).

Table 2: Mean and standard deviation of accuracy per condition, for the retrieved trials.

Mean (SD)	Accuracy	
	Low interference	High interference
Small	98.95 (1.73)	96.85 (5.44)
Large	96.64 (7.50)	93.18 (8.82)

Finally, we ran an Interference by Problem size repeated measures ANOVA on the percentage of retrieval use. A main effect of interference indicated that low interfering problems were more often solved by a retrieval strategy (mean (SE): 84.5 (4.0)) than high interfering problems (54.6 (5.4), $F(1,19) = 59.173$, $p < .001$, $\eta p^2 = .757$). Similarly, a main effect of problem size indicated that small problems were more often solved by a retrieval strategy (74.4 (4.6)) than large problems (64.6 (4.5), $F(1,19) = 12.908$, $p = .002$, $\eta p^2 = .405$). The interaction Interference x Problem size was not significant ($F < 1$).

3.2 Behavioral data in the multiplication production task (outside of the scanner)

Participants correctly solved on average 92.18% (SD = 4.54, range from 83 to 98%) of the problems in 1356 ms (mean of medians, SD = 484 ms , range from 743 to 2554). To permit a direct comparison with the task used in the scanning session, we report here analyses based only on the 24 problems (and commutative pairs) used in the 2×2 factorial design (see Appendix B for a regression analysis with all problems).

The 2x2 repeated measures ANOVA on the percentage of correct responses revealed a main effect of size ($F(1,19) = 10.632$, $p = .004$, $\eta_p^2 = .359$) indicating that small problems (mean (SE): 98 (.8)) were better performed than large problems (91.8 (1.7)). No effect of interference was found ($F(1,19) = 1.422$, $p = .248$, $\eta_p^2 = .070$). No interaction was found ($F < 1$).

The same analysis on the mean reaction time of correct responses revealed a main effect of interference ($F(1,19) = 30.075$, $p < .001$, $\eta_p^2 = .613$) indicating that low interfering problems (mean (SE): 1304 (121) msec) were more rapidly solved than high interfering ones (1961 (196) msec). A main effect of size ($F(1,19) = 19.316$, $p < .001$, $\eta_p^2 = .504$) showed that small problems (1305 (88) msec) were more rapidly solved than large problems (1960 (221) msec). There was also an interference × size interaction that just reached statistical significance ($F(1,19) = 4.472$, $p = .048$, $\eta_p^2 = .191$), showing that the interference effect was larger in large problems (mean difference: 854 msec) than in the small problems (mean difference: 459 msec). The interaction cannot be due to non-significant differences in matching mean problem size in the low and high interference groups, since this would predict an effect in the opposite direction to the one observed.

Importantly, the individual median reaction time in the production multiplication task highly correlated with the individual proportion of retrieval strategy used in the multiplication verification task in the scanner ($r(20) = -.830$). That is, the longer people took outside the scanner, the lower the proportion of questions solved using a retrieval strategy. Therefore the task carried out in the scanner appears to be a reliable test of multiplication fact problem solving.

3.3 Imaging data

First we detail the main effects of interference and problem size as tested by the 2 × 2 ANOVA. For these contrasts, we report effects that survive whole-brain family wise error (FWE) corrected thresholds at the peak level ($p < .05$). Subsequently, the main effect of strategy (retrieval versus non-retrieval) is reported. In this analysis (and in those detailed in the Appendix C) no voxel survived whole-brain FWE-corrected thresholds. Therefore, a less conservative threshold of $p < .001$ (uncorrected) was applied and activations that survived FWE correction at the cluster level are reported (required cluster size was 49 voxels). In the Appendix C, the interference and problem size effects are investigated using the retrieval trials only. For the sake of completeness, we also ran a parametric analysis which is reported in Appendix D.

3.3.1 Main effect of interference

Regions showing a significant main effect of interference are displayed in Table 3. The right cingulate, bilateral insula, right inferior frontal gyrus and left precentral gyrus all exhibited an increased BOLD response to more interfering problems. In contrast, only the left angular gyrus (posterior part) showed an effect in the opposite direction (i.e. a reduced BOLD response to more interfering problems). To reveal whether activity in these regions was modulated only by interference and not by problem size, a Bayesian analysis was conducted (Masson, 2011). Bayes factors (BFs) in favor of a null effect for problem size were calculated (i.e., no BOLD difference between large and small problems); values greater than 1 indicate more evidence in favor of the null effect while values less than 1 indicate that the brain region is also modulated by problem size. All the regions that showed an increased BOLD signal to more interfering problems also exhibited substantial evidence in favor of a problem size effect (all BFs < 0.0024; see percent signal change plots in Figure 2). In contrast, the cluster in the left angular gyrus that showed a significant reduction in BOLD activity to low versus high interference problems showed no evidence of a problem size effect. Here the evidence in favor of the null hypothesis (compared with evidence for a problem size effect) was 2.62 times in favor of the null, which is approaching a level of 3, generally considered to be substantial evidence in favor of the null (Dienes, 2011). Furthermore, the small numerical difference between large and small problems in the angular gyrus was in the opposite direction to that of high and low interfering problems (that is, on average, large problems elicited a greater BOLD response than small problems; see Figure 2). Therefore, we can be confident that task difficulty is not driving the change in BOLD activity.

Table 3: The interference effect in calculation on brain activation.

Main effect of Interference (*pFWE[peak]* < .05, *k* > 4)	*Peak voxel MNI Coordinates [x,y,z]*	*k*	*F*	*Z*
High > Low				
Left insula	[-30, +27, -03]	45	51.78	6.16
Right/left supplementary motor area and middle cingulate gyrus	[+3, +18, +48]	183	50.54	6.10
Right inferior frontal gyrus and insula lobe	[+33, +30, -03]	38	40.36	5.55
Left precentral gyrus and inferior frontal gyrus	[-39, +06, +30]	10	36.26	5.30
Low > High				
Left angular gyrus (PGp)	[-48, -72, +36]	16	42.72	5.69

3.3.2 Main effect of problem size

Regions showing a significant main effect of problem size are displayed in Table 4. Areas including the intraparietal sulcus and frontal lobes bilaterally were associated with an increased BOLD response to larger problems. Of these regions, a Bayesian analysis revealed that all but 2 also showed substantial evidence in favor of an interference effect (BFs < 0.15). However, in the right intraparietal sulcus the evidence was 2.64 times in favor of a null effect of interference, which is again approaching a level generally considered to be substantial evidence in favor of the null. In the left cerebellum, the evidence was 1.90 times in favor of a null effect of interference; which is weak evidence for the null hypothesis. No regions showed a reduced BOLD response to larger problems.

Table 4: Main effect of Problem size in calculation on brain activation.

Main effect of Size (*pFWE[peak]* < .05, *k* > 4)	*Peak voxel MNI Coordinates [x,y,z]*	*k*	*F*	*Z*
Large > Small				
Left intraparietal sulcus (hIP3/1)	[-33, -54, +42]	127	52.68	6.20
Left inferior frontal gyrus	[-48, +42, +15]	163	49.30	6.03
Left cerebellum	[-06, -78, -33]	23	43.50	5.73
Right inferior frontal gyrus and middle frontal gyrus	[+48, +36, +21]	47	41.93	5.64
Right/left supplementary motor area and superior medial gyrus	[+03, +27, +45]	61	39.81	5.52

Right intraparietal sulcus (hIP1/3)	[+39, -57, +45]	55	38.46	5.44
Left Insula lobe	[-30, +24, +00]	14	32.83	5.08

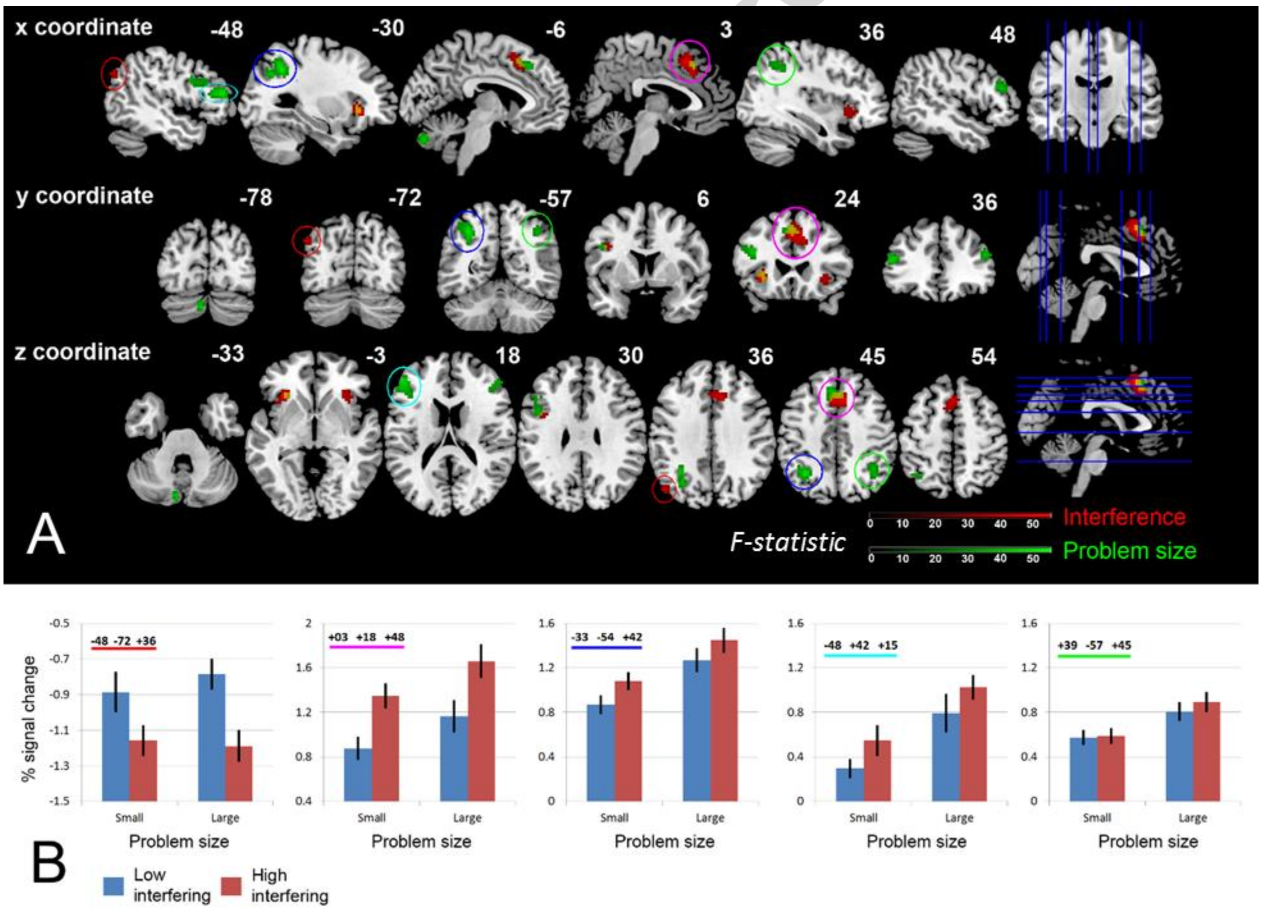


Figure 2: Main effect of interference (red), main effect of problem size (blue) and overlap of the two effects (yellow). Most of the activations present in Tables 3 and 4 are shown (panel A) as well as % signal change plots of the largest effects (panel B). Note the presence of a selective interference effect in the leftmost plot and a selective problem size effect in the rightmost plot.

3.3.3 Interactions between interference and problem size

No interaction effects were found anywhere in the brain, even at the lower threshold of p<0.001 (uncorrected) with FWE correction for cluster size.

3.3.4 Main effect of the retrieval strategy

In our analysis of the main effect of the strategy, four participants were excluded from the model because they used a retrieval strategy for more than 90% of trials. The effect of strategy (retrieval versus non-retrieval) on brain activation is displayed in Table 5. The use of a retrieval strategy led to greater activation in the left hippocampus, the bilateral rolandic operculi, bilateral cerebellar regions as well as the right amygdala, compared to problems solved by a non-retrieval strategy. One cluster was found in the mid-orbital white matter. Conversely, the left and right inferior frontal gyri, the right middle cingulate cortex, the right intraparietal sulcus, the right insula, the left inferior parietal cortex and the right middle frontal gyrus were more activate during non-retrieval trials than during retrieval trials.

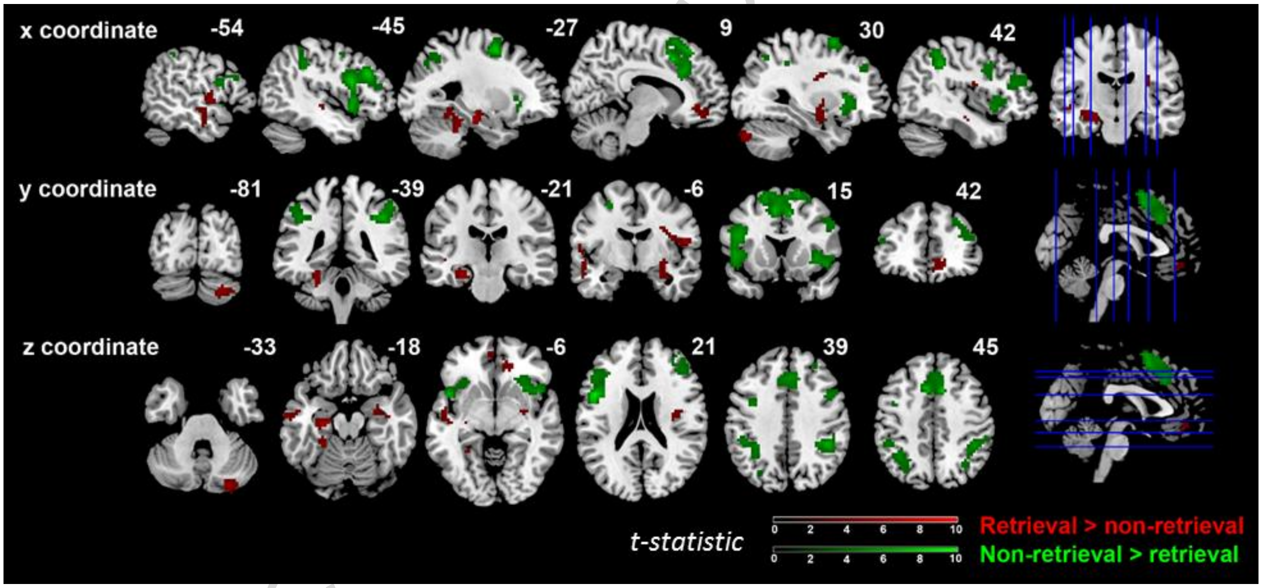


Figure 3: Activation map for the contrast of retrieval and non-retrieval (red = retrieved > non-retrieved; green = non-retrieved > retrieved).

Table 5: Main effect of Strategy (retrieval versus non-retrieval) on brain activation.

Main effect of Strategy (*p[unc]* < .001, *k* > 48)	*Peak voxel MNI Coordinates [x,y,z]*	k	Z	*t*
Retrieval > non-retrieval				
Left rolandic operculum	[-54, 0,+3]	93	4.03	5.55
Mid Orbital white matter	[+18, +42, -6]	83	3.97	5.41
Right rolandic operculum	[+51, -6, +18]	70	4.31	6.22
Right cerebellum	[+27, -81, -33]	68	4.06	5.62
Left hippocampus and parahippocampal gyrus	[-27, -21, -18]	61	4.43	6.52
Left cerebellum	[-27, -39, -30]	54	3.94	5.34
Right amygdala and hippocampus	[+30, -6, -9]	50	3.74	4.92

Non-retrieval > retrieval				
Right/left middle cingulate gyrus and supplementary motor area	[+9, +15, +45]	894	4.86	7.82
Left inferior frontal gyrus and insula lobe	[-48, +12, +21]	614	5.21	9.04
Right insula lobe	[+39, +18, +3]	255	4.15	5.83
Left inferior parietal cortex and intraparietal sulcus (hIP1/3)	[-45, -36, +42]	234	3.85	5.15
Right intraparietal sulcus (hIP 2)	[+42, -39, +39]	193	4.53	6.81
Right middle frontal gyrus	[+39, +39, +18]	154	3.83	5.11
Right inferior frontal gyrus	[+51, +12, +33]	76	3.92	5.29

Discussion

Interference occurs during the learning of multiplication tables, where problems that are more similar to previously learned problems are more difficult to memorize. This interference effect continues into adulthood and behavioral data have shown it to be independent of the well-characterized problem size effect (De Visscher & Noël, 2013, 2014a, 2014b). The present study investigated the brain regions associated with the interference effect in multiplication problems. In order to establish whether localized neural activity corresponds to the level of interference, rather than simply manipulation of task difficulty, both interference level and problem size were independently manipulated in our experimental design.

First, our results showed more activation for high interfering problems compared to low interfering problems in midline supplementary premotor and middle cingulate regions, in the left and right insula, in the left precentral gyrus and in the right inferior frontal gyrus. This network is characteristic of the set of regions that typically exhibit task-driven BOLD responses (Fox et al., 2005). Indeed, Bayes analyses revealed that in all of these regions there was strong evidence for modulation of BOLD activity by large versus small problems. Thus there is little evidence that these regions respond specifically to interference rather than more generally to task difficulty.

In contrast, a greater activation for low interfering problems than for high interfering problems was found in the left posterior angular gyrus. Importantly, a Bayes analysis revealed that within this region, problem size did not module BOLD activity and was most likely to be the same for both the large and small problems. The angular gyrus has been frequently reported in simple calculation tasks and is assumed to subserve the retrieval of arithmetic facts (Dehaene et al, 2003). Supporting this assumption, Grabner et al. (2009) reported higher activation in the left angular gyrus for the retrieval strategy compared to the procedural strategy. In the study of Stanescu-Cosson et al. (2000), the left angular gyrus was modulated by small problem size relative to large problem size, which could also reflect the retrieval strategy according to the assumption that retrieval is more used for small than for large problems (Zbrodoff & Logan, 2005). However, in our study, this region did not show greater activation for small versus large problems or for the retrieval strategy compared to the non-retrieval strategy.

More recently, Grabner et al. (2013) suggested that the angular gyrus could mediate the automatic mapping of arithmetic facts onto answers in long-term memory. In particular, they used a verification task with simple additions and multiplications. They contrasted two types of incorrect problems: confusion equations, i.e., incorrect equations in which the proposed answer is true for the other operation (9 x 6 = 15) and non-confusion equations (e.g., 9 x 6 = 52). The confusion effect has been attributed to the automatic activation of the incorrect arithmetic facts in memory and the need for further cognitive processing (Zbrodoff & Logan, 1986). Grabner and colleagues reasoned that if the left angular gyrus supports the automatic mapping of the operands of the problems and the associated solution, higher left angular gyrus activation should occur in the confusion (compared with non-confusion) equations. That is indeed what was observed. Results thus supported the mapping hypothesis according to which the left angular gyrus is activated when there is a mapping between symbols or chunks of symbols such as digits in arithmetic problems and their solutions (Ansari, 2008). This automatic mapping process assumption is also supported by a study by Wu et al. (2009) in which greater activation was found for problems presented in Arabic numerals compared to with roman numerals. In the context of the interference index used here, De Visscher and Noël (2014b) have shown that problems with a low interference index are more strongly encoded in long-term memory than those with a high interference index. Accordingly, the low-interfering problems would lead to a stronger mapping with their corresponding answers in memory and would thus lead to greater activation of the left angular gyrus, which is exactly what we observed.

Regarding the problem size effect, greater activation for larger problems compared to smaller problems was found in the left and right intraparietal sulci, in the left and right inferior frontal gyrus, the left cerebellum, the supplementary motor area and the left insula. Apart from the intraparietal sulci, activation differences in these regions are often seen when contrasting a more difficult with an easier task. Indeed, among these regions, only the right intraparietal sulcus was not modulated by interference and therefore demonstrated a "pure" problem size effect. This corroborates previous studies showing right or bilateral activation of the intraparietal sulcus in numerical tasks and suggests that this region supports the semantic representation of number magnitude (De Smedt et al., 2011; Stanescu-Cosson, Pinel, van de Moortele, et al., 2000). In the light of our finding of a specific problem size effect within the right intraparietal sulcus, and the proposal that this region plays a role in the semantic representation of number magnitude, we favor semantic representation interpretation (Campbell, 1995; Stoianov, Zorzi, Becker, & Umilta, 2002) of the problem size effect over other interpretations. According to Campbell's assumption, the problem size effect occurs because of the wider and fuzzier representation of larger answers compared to smaller answers (following the mental number line principle). Also in line with our findings, Stoianov, Zorzi, and Umiltà (2004) demonstrated the importance of the semantic representations in simple calculation by using a distributed associative network including semantic representations and symbolic representations. The machine was first trained on single-digit addition facts. Subsequently, they simulated different lesions and showed that the semantic representation was crucial in simple mental arithmetic, over the symbolic representation. Because problem size selectively modulated the right intraparietal sulcus, which is thought to support number magnitude representations, the semantic hypothesis better suits our findings than alternatives. As described in the introduction, one assumption is that the problem size effect is due to the fact that small problems are more frequent than large problems (Ashcraft, 1987; Ashcraft & Christy, 1995; McCloskey & Lindemann, 1992). Another suggestion is that large problems possess fewer consistent neighbors than small problems, and having consistent neighbors helps the retrieval of the response's problem (Verguts & Fias, 2005). Finally, Siegler (1988) argued that, throughout procedural strategy use, which developmentally precedes retrieval strategy use, more errors would have occurred when computing large problems than small ones, resulting in lower probabilities to retrieve the correct answer for large problems (Distribution of Association). These different explanations are not best placed to account for our finding that the problem size effect selectively modulated a region of the brain associated with representations of number magnitude.

Interestingly, left and right medial temporal regions, particularly the hippocampi, were found to be more activated when using a retrieval compared to a non-retrieval strategy (among other brain regions, see the Results section). In children, the left hippocampus was also found to be more active when retrieving arithmetic facts (De Smedt et al, 2011). This region is known to be involved in associative memory tasks (Eichenbaum et al., 2010; Squire, 1992; Yonelinas, 2002). In addition, a wide fronto-parietal network is involved during non-retrieval strategy, consistent with several previous studies (De Smedt, Holloway, & Ansari, 2011; Grabner et al., 2009; Stanescu-Cosson, Pinel, van De Moortele, et al., 2000; Zamarian, Semenza, Domahs, Benke, & Delazer, 2007).

Regarding atypical development, structural and functional differences in the activation of the angular gyrus and the intraparietal sulci have been reported in children with dyscalculia (math learning disability, see Kaufmann, Kucian, & von Aster, in press for a review). In the context of heterogeneous profiles in dyscalculia, future studies could contrast two well-known profiles: arithmetic facts dyscalculia, where a specific deficit is found in arithmetic facts retrieval, and pure dyscalculia, where a deficit of the number sense is present. On the basis of our findings, we might predict that structural and/or functional differences should be found in the angular gyrus (or the hippocampus) in individuals with arithmetic facts dyscalculia whereas differences in the intraparietal sulci should be found in individuals with a pure dyscalculia profile.

4. Conclusions

In summary, this study shows how interference affects the processing of arithmetic facts. In addition to replicating previous behavioral findings, we identified a region of the left angular gyrus where activity was modulated by interference but not by differences in problem size. Interestingly, a large network of regions were associated with both the interference effect and the problem size effect, indicating that activity in these regions was being largely driven by differences in difficulty between experimental conditions. Nevertheless, activity in the right intraparietal sulcus was modulated by problem size but not by high- versus low-interfering problems. This supports the proposal that this region subserves the magnitude representation of numbers. These results not only further our understanding of how the brain carries out the essential function of mathematical cognition, but provide strong predictions about patterns of disordered mathematical cognition as well.

Appendix A: Stimuli

	LOW INTERFERING				HIGH INTERFERING			
	Problem	Size (product)	Interference level	False answer (distance)	Problem	Size (product)	Interference level	False answer (distance)
SMALL	2x7=	14	4	12 (2)	3x6=	18	8	15 (3)
	9x2=	18	7	16 (2)	5x4=	20	8	16 (4)
	5x5=	25	3	30 (5)	4x3=	12	10	15 (5)
	4x4=	16	5	20 (4)	4x6=	24	12	28 (4)
	2x8=	16	7	18 (2)	3x7=	21	13	24 (3)
	2x6=	12	3	10 (2)	8x3=	24	13	21 (3)
mean		16.8	4.8			19.8	10.7	
LARGE	6x6=	36	4	30 (6)	3x9=	27	9	24 (3)
	6x5=	30	6	36 (6)	9x4=	36	9	32 (4)
	5x9=	45	6	40 (5)	8x5=	40	9	45 (5)
	9x9=	81	6	72 (9)	7x8=	56	9	63 (7)
	5x7=	35	7	40 (5)	6x7=	42	22	48 (4)
	7x7=	49	7	56 (7)	4x8=	32	25	28 (4)
mean		46	6			38.8	10	

Where “distance” is the absolute difference between the false answer and the product of the problem.

Appendix B : Regression analyses on the behavioral task conducted outside of the scanner.

The interference effect and the problem size effect were tested using a multiple regression with mean reaction time as the dependent variable. "Interference" (interference parameter, De Visscher & Noël, 2014b) and "problem size" (product of the problem) were entered as separate factors into a multiple regression. Both factors were significant and explained together 52.1% of the variance (interference factor: $t(63) = 2.425$, $p = .018$, problem size factor: $t(63) = 5.078$, $p < .001$). This replicates previous results showing that both problem size and the interference parameter make unique contributions to multiplication difficulty.

Appendix C: analyses on the retrieved trials only

In this 2x2 ANOVA , we tested the main effect of interference and the main effect of the problem size only on the trials that were retrieved. When people retrieved the answer from long-term memory, the right superior medial frontal gyrus, and the right anterior insula showed higher activation for high interfering problems than for low interfering problems. Interestingly, a higher activation for the low interfering problems than for the high interfering ones is shown in the bilateral posterior part of the angular gyrus.

Main effect of Interference (*p[unc]* < .001, *k* > 48)	*Peak voxel MNI Coordinates [x,y,z]*	*k*	*F*	*Z*
High > Low				
Right superior medial gyrus	[+09, +24, +42]	229	32.94	5.08
Right anterior insula	[+36, +24, -06]	84	25.55	4.53
Low > High				
Right angular gyrus (PGp)	[+48, -63 +27]	50	23.42	4.35
Left angular gyrus (PGp)	[-45, -63, +24]	53	20.54	4.09

Regarding the problem size, the larger problems activated more the left and right intraparietal sulci, the right superior medial frontal gyrus, the right middle frontal gyrus, the left cerebellum as well as the left inferior frontal gyrus.

Main effect of Size (*p[unc]* < .001, *k* > 48)	*Peak voxel MNI Coordinates [x,y,z]*	*k*	*F*	*Z*
Large > Small				
Left intraparietal sulcus (hIP3/1)	[-33, -54, +39]	324	45.08	5.80
Right superior medial gyrus	[+03, +27, +45]	220	36.97	5.35
Right middle frontal gyrus	[+42, +30, +21]	280	35.47	5.25
Left cerebellum	[-06, -78, -30]	95	33.93	5.15
Left inferior frontal gyrus	[-51, +30, +15]	599	30.01	4.88
Right intraparietal sulcus (hIP1/3)	[+33, -48, +45]	193	26.80	4.63
Right middle frontal gyrus	[+36, +57, +06]	105	17.41	3.78

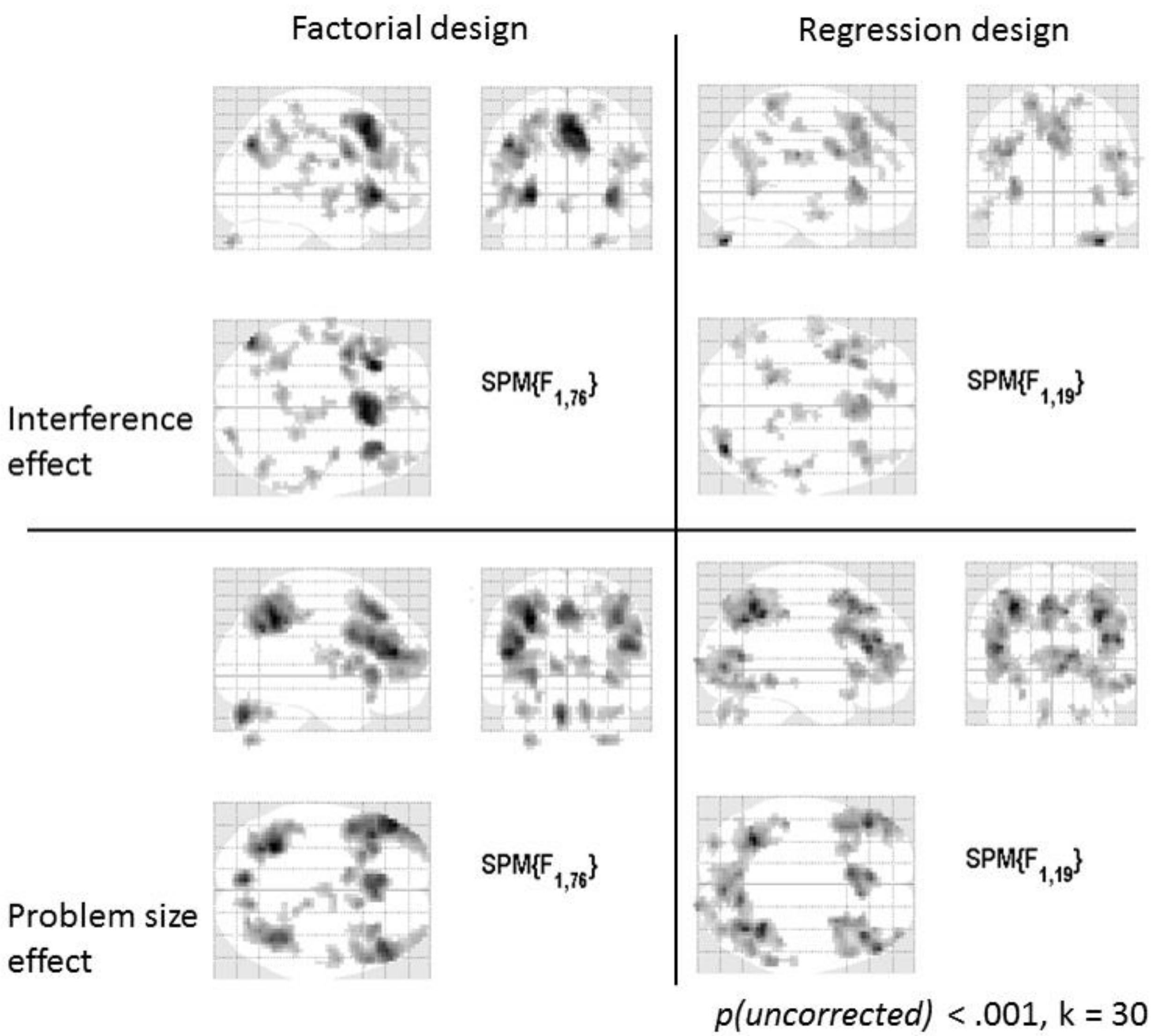
No interaction effects were found anywhere in the brain, even at the lower threshold of $p<0.001$ (uncorrected) with FWE correction for cluster size.

Appendix D: Parametric analysis of the Interference effect and Problem size effect on BOLD modulation

Since there is a correlation between problem size and interference level in the set of naturally learned arithmetic problems, we carefully selected problems to fall into a 2x2 factorial design so that each factor could be orthogonally manipulated. Having decided on the factorial design we generated a jittered sequence of trial types suitable for optimizing the differences in the hemodynamic response for each of the 4 trial types. Consequently, a parametric analysis of our imaging data is not optimal for three reasons: first, the ITIs were not optimized for this analysis, second, the problems were selected to fall within the cells of the factorial design rather than cover the full range of possible values, and third, a parametric design would not be as sensitive to interaction effects because the relationship between problem size and interference changes with problem size.

For the sake of completeness and in order to compare the two analyses, we ran a parametric analysis. The results of the main effects from the factorial analysis and the parametric analysis are shown as “glass brain” images so that all suprathreshold voxels are visible (Figure 4). We present the results at an uncorrected threshold of $p < .001$ and $k = 30$, since the results from the regression analysis do not survive FWE correction at the peak level. This likely reflects the lack of power for this analysis. In both analyses no interactions were found anywhere in the brain. However, for the main effects, activation patterns are qualitatively very similar across analyses. The regression analysis did identify some visual cortical regions, not highlighted by the factorial analysis, where BOLD correlated with problem size. These correlations were not predicted a priori and do not survive FWE, so are difficult to interpret.

Figure 4: Comparison of the factorial analysis and the parametric analysis including the both factors Interference parameter and Problem size.


Factorial design
Regression design
Interference effect
SPM{F 1,76}
SPM{F 1,19}
Problem size effect
SPM{F 1,76}
SPM{F 1,19}
p(uncorrected) < .001, k = 30

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References

Ansari, D. (2008). Effects of development and enculturation on number representation in the brain. *Nature Reviews. Neuroscience*, *9*, 278–291. doi:10.1038/nrn2334

Ashcraft, M. H. (1987). Children's Knowledge of Simple Arithmetic: A Developmental Model and Simulation. In J. Bisanz, C. Brainerd, & R. Kail (Eds.), *Formal Methods in Developmental Psychology SE - 9* (pp. 302–338). Springer New York. doi:10.1007/978-1-4612-4694-7_9

Ashcraft, M. H., & Christy, K. S. (1995). The frequency of arithmetic facts in elementary texts: Addition and multiplication in Grades 1-6. *Journal for Research in Mathematics Education*, *26*(5), 396–421.

Campbell, J. I. D. (1995). Mechanisms of simple addition and multiplication: A modified network-interference theory and simulation. *Mathematical Cognition*, *1*(2), 121–164.

Cho, S., Metcalfe, A., Young, C., Ryali, S., Geary, D. C., & Menon, V. (2012). Hippocampal–Prefrontal Engagement and Dynamic Causal Interactions in the Maturation of Children's Fact Retrieval. *Journal of Cognitive …*, *24*(9), 1849–1866. doi:10.1162/jocn

Cox, R. W. (1996). AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research, an International Journal*, *29*(3), 162–73. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8812068

De Brauwer, J., Verguts, T., & Fias, W. (2006). The representation of multiplication facts: Developmental changes in the problem size, five, and tie effects. *Journal of Experimental Child Psychology*, *94*(1), 43–56. doi:http://dx.doi.org/10.1016/j.jecp.2005.11.004

De Smedt, B., Holloway, I. D., & Ansari, D. (2011). Effects of problem size and arithmetic operation on brain activation during calculation in children with varying levels of arithmetical fluency. *NeuroImage*, *57*(3), 771–781. Retrieved from http://www.scopus.com/inward/record.url?eid=2-s2.0-79959699116&partnerID=40&md5=0fbe4454eccca3417f2e5b5e1295695b

De Smedt, B., Holloway, I. D., & Ansari, D. (2011). Effects of problem size and arithmetic operation on brain activation during calculation in children with varying levels of arithmetical fluency. *NeuroImage*, *57*(3), 771–81. doi:10.1016/j.neuroimage.2010.12.037

De Visscher, A., & Noël, M.-P. (2013). A case study of arithmetic facts dyscalculia caused by a hypersensitivity-to-interference in memory. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *49*(1), 50–70. doi:10.1016/j.cortex.2012.01.003

De Visscher, A., & Noël, M.-P. (2014a). Arithmetic facts storage deficit: the hypersensitivity-to-interference in memory hypothesis. *Developmental Science*. doi:10.1111/desc.12135

De Visscher, A., & Noël, M.-P. (2014b). The detrimental effect of interference in multiplication facts storing: Typical development and individual differencse. *Journal of Experimental Psychology: General*, *143*(6), 2380–2400.

Dehaene, S. (1992). Varieties of Numerical Abilities. *Cognition*, *44*(1-2), 1–42. Retrieved from <Go to ISI>://A1992JG78100001

Dehaene, S., Piazza, M., Pinel, P., & Cohen, L. (2003). Three parietal circuits for number processing. *Cognitive Neuropsychology*, *20*(3-6), 487–506. Retrieved from <Go to ISI>://000184129000012

Delazer, M., Domahs, F., Bartha, L., Brenneis, C., Lochy, a, Trieb, T., & Benke, T. (2003). Learning complex arithmetic—an fMRI study. *Cognitive Brain Research*, *18*(1), 76–88. doi:10.1016/j.cogbrainres.2003.09.005

Dienes, Z. (2011). Bayesian versus Orthodox statistics: Which side are you on? *Perspectives on Psychological Science*, *6*(3), 274–290.

Eichenbaum, H., Otto, T., & Cohen, N. J. (2010). Two functional components of the hippocampal memory system. *Behavioral and Brain Sciences*, *17*(03), 449–472. doi:10.1017/S0140525X00035391

Eickhoff, S. B., Stephan, K. E., Mohlberg, H., Grefkes, C., Fink, G. R., Amunts, K., & Zilles, K. (2005). A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *NeuroImage*, *25*, 1325–1335. doi:10.1016/j.neuroimage.2004.12.034

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences of the United States of America*, *102*, 9673–9678. doi:10.1073/pnas.0504136102

Giovanello, K. S., Schnyer, D., & Verfaellie, M. (2009). Distinct hippocampal regions make unique contributions to relational memory. *Hippocampus*, *19*(2), 111–7. doi:10.1002/hipo.20491

Grabner, R., Ansari, D., Koschutnig, K., Reishofer, G., & Ebner, F. (2013). The function of the left angular gyrus in mental arithmetic: evidence from the associative confusion effect. *Human Brain Mapping*, *34*(5), 1013–24. doi:10.1002/hbm.21489

Grabner, R. H., Ansari, D., Koschutnig, K., Reishofer, G., Ebner, F., & Neuper, C. (2009). To retrieve or to calculate? Left angular gyrus mediates the retrieval of arithmetic facts during problem solving. *Neuropsychologia*, *47*(2), 604–608. doi:DOI 10.1016/j.neuropsychologia.2008.10.013

Ischebeck, A., Zamarian, L., Siedentopf, C., Koppelstätter, F., Benke, T., Felber, S., & Delazer, M. (2006). How specifically do we learn? Imaging the learning of multiplication and subtraction. *NeuroImage*, *30*(4), 1365–75. doi:10.1016/j.neuroimage.2005.11.016

Jordan, N. C., & Montani, T. O. (1997). Cognitive arithmetic and problem solving: A comparison of children with specific and general mathematics difficulties. *Journal of Learning Disabilities*, *30*(6), 624–&. Retrieved from <Go to ISI>://A1997YF26400006

Kaufmann, L., Kucian, K., & von Aster, M. (n.d.). Brain Correlates of Numerical Disabilities - Oxford Handbooks. In R. Cohen Kadosh & A. Dowke (Eds.), *The Oxford Handbook of Mathematical Cognition*. Oxford Handbook. Retrieved from http://www.oxfordhandbooks.com/view/10.1093/oxfordhb/9780199642342.001.0001/oxfordhb-9780199642342-e-009?rskey=1iiv9m&result=5

Masson, M. E. J. (2011). A tutorial on a practical Bayesian alternative to null-hypothesis significance testing. *Behavior Research Methods*, *43*, 679–690. doi:10.3758/s13428-011-0126-4

McCloskey, M., Harley, W., & Sokol, S. M. (1991). Models of arithmetic fact retrieval: An evaluation in light of findings from normal and brain-damaged subjects. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *17*(3), 377–397. doi:10.1037//0278-7393.17.3.377

McCloskey, M., & Lindemann, A. M. (1992). Mathnet: Preliminary results from a distributed model of arithmetic fact retrieval. In J. I. D. Campbell (Ed.), *The nature and origins of mathematical skills* (Elsevier., pp. 365–409).

Menon, V. (2014). Arithmetic in the child and adult brain. In R. Cohen Kadosh & A. Dowker (Eds.), *The Oxford Handbook of Mathematical Cognition* (Oxford Uni.).

Nairne, J. S. (1990). A feature model of immediate memory. *Memory & Cognition*, *18*(3), 251–269.

Robinson, K. M., Arbuthnott, K. D., Rose, D., McCarron, M. C., Globa, C. a, & Phonexay, S. D. (2006). Stability and change in children's division strategies. *Journal of Experimental Child Psychology*, *93*(3), 224–38. doi:10.1016/j.jecp.2005.09.002

Roussel, J.-L., Fayol, M., & Barrouillet, P. (2002). Procedural vs. direct retrieval strategies in arithmetic: A comparison between additive and multiplicative problem solving. *European Journal of Cognitive Psychology*, *14*(1), 61–104. doi:10.1080/09541440042000115

Siegler, R. S. (1988). Strategy choice procedures and the development of multiplication skill. *Journal of Experimental Psychology: General*, *117*, 258–275.

Squire, L. R. (1992). Memory and the hippocampus: A synthesis from findings with rats, monkeys, and humans. *Psychological Review*, *99*(2), 195–231. doi:10.1037//0033-295X.99.2.195

Stanescu-Cosson, R., Pinel, P., van de Moortele, P. F., Le Bihan, D., Cohen, L., & Dehaene, S. (2000). Understanding dissociations in dyscalculia - A brain imaging study of the impact of number size on the cerebral networks for exact and approximate calculation. *Brain*, *123*, 2240–2255. Retrieved from <Go to ISI>://000165413200006

Stanescu-Cosson, R., Pinel, P., van De Moortele, P. F., Le Bihan, D., Cohen, L., & Dehaene, S. (2000). Understanding dissociations in dyscalculia: a brain imaging study of the impact of number size on the cerebral networks for exact and approximate calculation. *Brain : A Journal of Neurology*, *123 (Pt 1*, 2240–55. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11050024

Stoianov, I., Zorzi, M., Becker, S., & Umilta, C. (2002). Associative Arithmetic with Boltzmann Machines : the Role of Number Representations Mean-Field BMs with Contrastive Divergence Learning. *Lecture Notes in Computer Science*, *2415*, 277–283.

Stoianov, I., Zorzi, M., & Umiltà, C. (2004). The role of semantic and symbolic representations in arithmetic processing: insights from simulated dyscalculia in a connectionist model. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *40*, 194–196. doi:10.1016/S0010-9452(08)70948-1

Thevenot, C., Castel, C., Fanget, M., & Fayol, M. (2010). Mental subtraction in high- and lower skilled arithmetic problem solvers: verbal report versus operand-recognition paradigms. *Journal of Experimental Psychology. Learning, Memory, and Cognition*, *36*(5), 1242–55. doi:10.1037/a0020447

Verguts, T., & Fias, W. (2005). Interacting neighbors: a connectionist model of retrieval in single-digit multiplication. *Memory & Cognition*, *33*(1), 1–16. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15915789

Wu, S. S., Chang, T. T., Majid, a, Caspers, S., Eickhoff, S. B., & Menon, V. (2009). Functional heterogeneity of inferior parietal cortex during mathematical cognition assessed with cytoarchitectonic probability maps. *Cerebral Cortex (New York, N.Y. : 1991)*, *19*(12), 2930–45. doi:10.1093/cercor/bhp063

Yonelinas, A. P. (2002). The nature of recollection and familiarity: A review of 30 years of research. *Journal of Memory and Language*, *46*(3), 441–517. doi:DOI 10.1006/jmla.2002.2864

Zamarian, L., Semenza, C., Domahs, F., Benke, T., & Delazer, M. (2007). Alzheimer's disease and mild cognitive impairment: Effects of shifting and interference in simple arithmetic. *Journal of the Neurological Sciences*, *263*(1-2), 79–88. doi:DOI 10.1016/j.jns.2007.06.005

Zbrodoff, N. J., & Logan, G. D. (1986). On the autonomy of mental processes: a case study of arithmetic. *Journal of Experimental Psychology. General*, *115*(2), 118–30. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/2940313

Zbrodoff, N. J., & Logan, G. D. (2005). What everyone finds: The problem-size effect. In J. I. D. Campbell (Ed.), *Handbook of Mathematical Cognition*.

Interference effect in arithmetic fact: an fMRI study

Highlights

- We investigate the brain regions underpinning arithmetic fact solving using fMRI

- The recently-described interference effect is contrasted with problem size

- Brain regions are identified responding uniquely to interference and problem size

- These results suggest that the two effects are behaviourally and neurally distinct

- Our findings refine current models of the biological basis of mathematical cognition